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Approved by	[Approver name, title, and affiliation]	Date:

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 05/18/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47434101 Mayer, T.; Hampton, R. (2008) Mesotrione - Magnitude of the Residues in or on Soybean. Lab Project Number: T005595-06. Study No. 2K8-901-6005595-06. Unpublished study prepared by Syngenta Crop Protection, Inc. 209 p.

EXECUTIVE SUMMARY:

Syngenta Crop protection has submitted a processing study for mesotrione on soybean. In a single trial conducted in AR during the 2007 growing season, a single application of a 4 lb/gal suspension concentrate (SC) formulation was made to the soil at planting to two treatment plots at 0.190 lb ai/A and at an exaggerated rate of 0.951 lb ai/A (~5x). The applications were made in spray volumes of ~10 gal/A of water using ground equipment; no adjuvant was added to the spray mixtures. Mature soybean seed was harvested at commercial maturity, 113 days after treatment/planting, and processed into hulls, meal, and refined oil. We note that samples of aspirated grain fractions were not generated in conjunction with the processed commodities; however, because the study use pattern reflected at-planting application to soybean, no residue data for aspirated grain fractions are required.

Residues of mesotrione and its metabolite MNBA [4-(methylsulfonyl)-2-nitrobenzoic acid] in/on soybean seed, hulls, meal, and refined oil were determined using Syngenta Method RAM 366/01, a high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS). The method is adequate for data collection based on acceptable concurrent method recoveries. The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices.

Soybean seed samples were stored frozen for 6.6 months prior to analysis. Following generation of processed commodities, samples of hulls, meal, and oil were stored frozen for up to 5.9

months. Adequate storage stability data are available to support the storage conditions and durations of samples of soybean seed (RAC). No data are available reflecting the storage stability of residues of mesotrione in any processed commodity. Because no residues were detected in/on soybean seed treated at 5x from the processing study or in any processed commodities, and the petitioner has adequately demonstrated the stability of residues in soybean seed, no additional storage data are required.

Following application of the 4 lb/gal SC formulation at planting at 0.190 lb ai/A and 0.951 lb ai/A/application (~5x), residues of mesotrione and MNBA were both below the LOQ (<0.01 ppm) in/on all samples of soybean seed and the processed commodities of hulls, meal, and refined oil. Because residues were below the LOQ in all samples, processing factors could not be calculated.

The theoretical concentration factors for soybean, based on separation into components, are 11.3x for soybean hulls, 2.2x for soybean meal, and 12.0x for soybean oil (OPPTS 860.1520, Table 3).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP# 358159.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Mesotrione is a triketone herbicide which inhibits the enzyme *p*-hydroxyphenyl-pyruvate dioxygenase (HPPD), disrupting carotenoid biosynthesis. This process leads to the destruction of chlorophyll, resulting in a bleaching effect in susceptible plants. Mesotrione is intended for preemergence and postemergence use for the selective control of annual broadleaf weeds. Mesotrione is currently registered for use on asparagus; field, pop, and sweet corn; cranberry, bush and caneberries; flax; grasses grown for seed; millet; oats; okra; rhubarb; sorghum; and sugarcane. Under PP#8F7456, Syngenta Crop Protection is proposing to add use on soybean.

The chemical structure and nomenclature of mesotrione and its metabolite MNBA, and the physicochemical properties of the technical grade of mesotrione are presented in Tables A.1 and A.2.

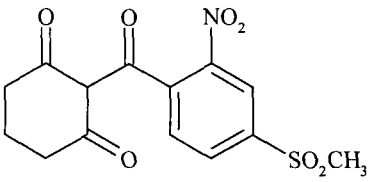
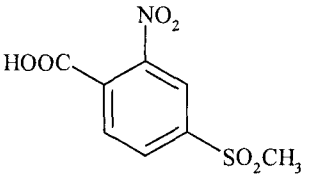
TABLE A.1. Test Compound Nomenclature.	
Chemical structure	
Common name	Mesotrione
Company experimental name	ZA1296
IUPAC name	2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione
CAS name	2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione
CAS registry number	104206-82-8
End-use product (EP)	4 lb/gal SC (Callisto® Herbicide; EPA Reg. No. 100-1131)
Compound	
Common name	MNBA
Chemical name	4-(methylsulfonyl)-2-nitrobenzoic acid

TABLE A.2. Physicochemical Properties of the Technical Grade Test Compound Mesotrione.		
Parameter	Value	Reference
Melting point/range	148.7-152.5°C	RD Memo, H. Podall, 2/24/2000; DP#: 263245.
pH	3.4 (1% dispersion in water; 25°C)	
Density	1.46 g/mL, 20°C	
Water solubility	20°C 160 ppm, unbuffered water 0.22 g/100 mL, pH 4.8 1.5 g/100mL, pH 6.9 2.2 g/100 mL, pH 9	
Solvent solubility	20°C 0.37 g/100 mL, methanol 1.7 g/100 mL, ethyl acetate 0.27 g/100 mL, toluene 10.4 g/100 mL, acetonitrile <0.03 g/100 mL, heptane 8.1 g/100 mL, acetone	
Vapor pressure	4.3×10^{-8} torr, 20°C	
Dissociation constant, pK_a	3.12, 20°C	
Octanol/water partition coefficient, Log(K_{OW})	20°C log P_{OW} = 0.11 in unbuffered water log P_{OW} = 0.90 in pH 5 buffer log P_{OW} <-1 at pH 7 and 9 buffered water	
UV/visible absorption spectrum	Absorption maximum in methanol at 256 mu, with a molar extinction coefficient of 2.24 x 104 M cm.	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a single trial conducted in AR during the 2007 growing season, a single application of a 4 lb/gal SC formulation was made to the soil at planting to two treatment plots at 0.190 lb ai/A and at an exaggerated rate of 0.951 lb ai/A (~5x). The applications were made in spray volumes of ~10 gal/A of water using ground equipment; no adjuvant was added to the spray mixtures. Mature soybean seed was harvested at commercial maturity, 113 days after treatment/planting and processed into hulls, meal, and refined oil. Details of the study use pattern are presented in Table B.1.1.

Monthly rainfall and temperature ranges were provided for each site, along with the maintenance pesticides and fertilizers that were used. The petitioner stated that actual temperature recordings and rainfall averages were within average historical values for the residue study period.

TABLE B.1.1. Study Use Pattern.

Trial Identification: City, State; Year; Trial No.	EP[1]	Application				Tank Mix Adjuvants
		Method/Timing	Volume (gal/A) [L/ha]	Rate (lb ai/A) [g ai/ha]	Total Rate (lb ai/A) [g ai/ha]	
Proctor, AR; 2007; C24AR078244	4 lb/gal SC	1. Soil surface spray at planting	10.1 [96]	0.190 [213]	0.190 [213]	None
		1. Soil surface spray at planting	10.1 [96]	0.951 [1065]	0.951 [1065]	

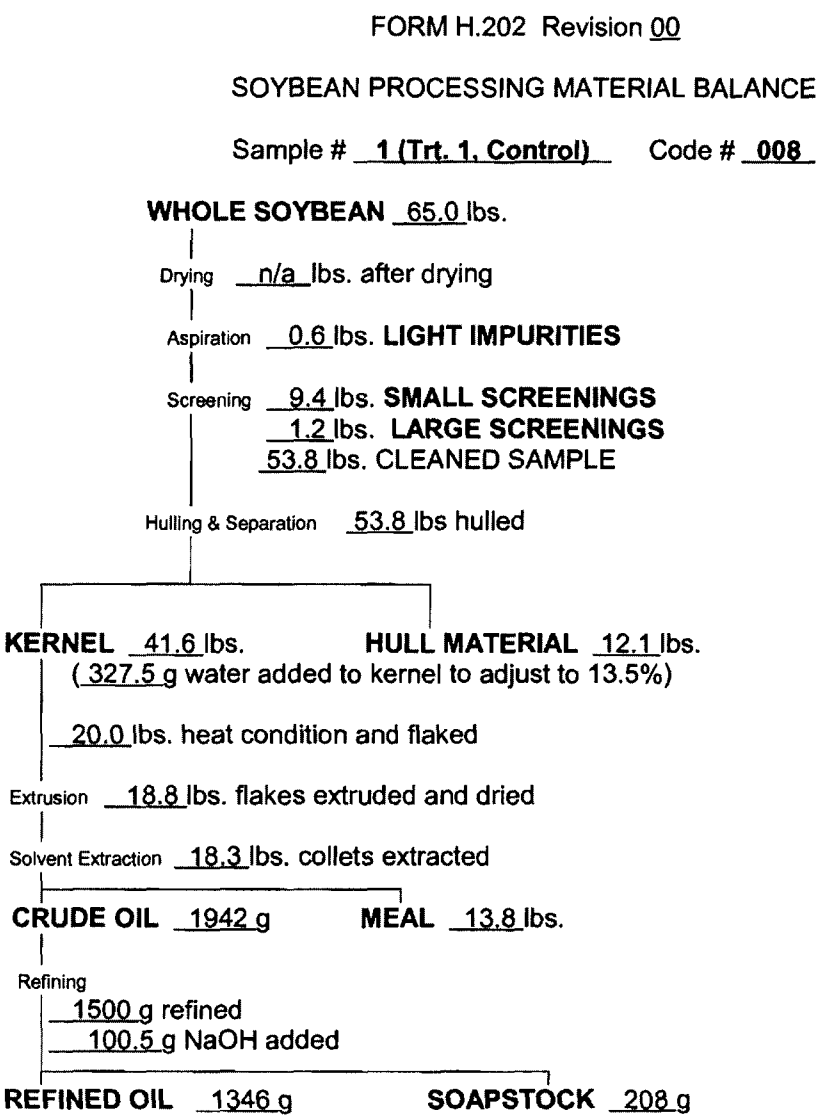
[1] EP = End-use Product

B.2. Sample Handling and Processing Procedures

A single bulk (~65 lb) control sample and one bulk treated sample from each treatment plot were collected at commercial maturity, 113 days after treatment/planting. No details were supplied concerning sample storage at the field site. Samples were shipped via FedEx at ambient temperature from the field site to the processing facility, GLP Technologies (Navasota, TX) within 5 days of harvest.

At GLP Technologies, samples were placed in frozen storage (≤-6 °C) until processing. Bulk seed was processed using simulated commercial procedures into hulls, meal, and refined oil. Processing was initiated 45 days after harvest and was completed within 54 days of harvest. The petitioner provided a detailed description of the processing procedures, along with flow charts with material balance information; see Figure B.2.1, which was copied without alteration from MRID 47434101. The unprocessed soybean seed and processed commodities were placed in frozen storage for 5 days following completion of processing, after which they were packed in dry ice and shipped to Syngenta Crop Protection (Greensboro, NC) via FedEx. Samples were subsequently shipped from Syngenta to the analytical laboratory, ADPEN Laboratories (Jacksonville, FL), where they were stored frozen (-29.5 to -3.5 °C) until analysis.

FIGURE B.2.1. Processing Flowchart for Soybean.



B.3. Analytical Methodology

Residues of mesotrione and its metabolite MNBA in/on soybean seed, hulls, meal, and refined oil were determined using LC/MS/MS Method RAM 366/01 with minor modifications. This method was previously forwarded to the U.S. Food and Drug Administration for inclusion in the Pesticide Analytical Manual Volume II as a confirmatory method.

Briefly, samples were extracted with acetonitrile:water (1:1, v:v) containing sodium chloride, then centrifuged. An aliquot of the extract was diluted with water for analysis by LC/MS/MS. For analysis of MNBA, the diluted aliquot was passed through a silica gel solid phase extraction

column prior to LC/MS/MS analysis. The monitored ion transitions were 338 → 291 for mesotrione and 244 → 142 for MNBA. The LOQ was 0.01 ppm for both analytes; the method limit of detection (LOD) was not reported.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2. Soybean seed samples were stored frozen for 6.6 months prior to analysis. Following generation of processed commodities, samples of hulls, meal, and oil were stored frozen for up to 5.9 months. Storage stability data are available (DP#s 245477 and 260267, 6/6/2001, S. Levy) which indicate that residues of mesotrione and MNBA are stable under frozen storage conditions in/on soybean seed for up to 40 months. The available storage stability data are adequate to support the storage durations and conditions of samples of soybean seed (RAC). No data are available reflecting the storage stability of residues of mesotrione in any processed commodity. Because no residues were detected in/on soybean seed treated at 5x from the processing study or in any processed commodities, and the petitioner has adequately demonstrated the stability of residues in soybean seed, no additional storage data are required.

Concurrent method recovery data are presented in Table C.1. The LC/MS/MS Method RAM 366/01 was adequate for data collection based on acceptable concurrent method recovery data. Recoveries were generally within the acceptable range of 70-120% for all samples of soybean seed and processed commodities fortified with mesotrione or MNBA at 0.01 and 0.10 ppm each. Apparent residues of mesotrione and MNBA were below the LOQ (<0.01 ppm) in/on one sample each of untreated soybean seed, meal, hulls and refined oil.

Residue data from the soybean processing study are reported in Table C.3. Following application of the 4 lb/gal SC formulation at planting at 0.190 lb ai/A and 0.951 lb ai/A (~5x), residues of mesotrione and MNBA were both below the LOQ (<0.01 ppm) in/on all samples of soybean seed and the processed commodities of hulls, meal, and refined oil. Because residues were below the LOQ in all samples, processing factors could not be calculated.

The theoretical concentration factors for soybean, based on separation into components, are 11.3x for soybean hulls, 2.2x for soybean meal, and 12.0x for soybean oil (OPPTS 860.1520, Table 3).

TABLE C.1. Summary of Concurrent Recoveries of Mesotrione and its Metabolite, MNBA, from Soybean Seed and Processed Fractions.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± Std. Dev.[1]
Mesotrione				
Soybean seed	0.01	6	104.0, 103.2, 131.6, 111.6, 122.6, 110.2	113.9 ± 11.1
	0.10	6	96.6, 94.8, 132.6, 111.0, 111.2, 99.2	107.6 ± 14.2
Soybean hulls	0.01	1	106.8	NA
	0.10	1	122.1	NA

TABLE C.1. Summary of Concurrent Recoveries of Mesotrione and its Metabolite, MNBA, from Soybean Seed and Processed Fractions.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± Std. Dev.[1]
Soybean meal	0.01	1	114.4	NA
	0.10	1	113.3	NA
Refined oil	0.01	1	134.0	NA
	0.10	1	100.4	NA
MNBA				
Soybean seed	0.01	6	90.2, 89.2, 110.8, 106.4, 100.6, 124.6	103.6 ± 13.4
	0.10	6	101.0, 94.2, 101.2, 108.6, 93.6, 98.8	99.6 ± 5.5
Soybean hulls	0.01	1	97.0	NA
	0.10	1	95.3	NA
Soybean meal	0.01	1	126.4	NA
	0.10	1	102.2	NA
Refined oil	0.01	1	108.8	NA
	0.10	1	107.6	NA

[1] NA = Not applicable; standard deviation is only calculated for sample sizes ≥3.

TABLE C.2. Summary of Storage Conditions

Matrix	Storage Temperature (°C)	Actual Maximum Storage Duration[1]	Interval of Demonstrated Storage Stability (months)
Soybean seed	-18 ± 5	201 days (6.6 months)	Residues of mesotrione and MNBA are stable under frozen storage conditions in/on soybean seed for up to 40 months.[2]
Soybean hulls		178 days (5.9 months)	None required because residues were <LOQ in/on soybean seed treated at 5x and in all processed commodities.
Soybean meal			
Soybean refined oil			

[1] Interval from harvest to extraction; seed samples were analyzed on the day of extraction, and processing samples were analyzed within 16 days of extraction.
[2] Memo, S. Levy, 6/6/2001; DP#s: 245477 and 260267

TABLE C.3. Residue Data from Soybean Processing Study with Mesotrione.

RAC	Processed Commodity	Total Rate (lb ai/A) [g ai/ha]	DAP[1] (days)	Residues (ppm)		Processing Factor[2]	
				Mesotrione	MNBA	Mesotrione	MNBA
Soybean seed	Seed (RAC)	0.190 [213]	113	<0.01	<0.01	--	--
	Hulls			<0.01	<0.01	NC	NC
	Meal			<0.01	<0.01	NC	NC
	Refined oil			<0.01	<0.01	NC	NC
Soybean seed	Seed (RAC)	0.951 [1065]	113	<0.01	<0.01	--	--
	Hulls			<0.01	<0.01	NC	NC
	Meal			<0.01	<0.01	NC	NC
	Refined oil			<0.01	<0.01	NC	NC

[1] DAP = Days after planting.
[2] NC = Not calculated because residues were nonquantifiable in both the RAC and processed commodity.

D. CONCLUSION

The submitted soybean processing study is acceptable, and indicates that residues of mesotrione do not appear to concentrate in the soybean processed commodities of hulls, meal, and refined oil. Following application of a 4 lb/gal SC formulation made to the soil at planting at 0.190 lb ai/A and 0.951 lb ai/A (~5x), residues of mesotrione and MNBA were each below the LOQ (<0.01 ppm) in/on all samples of soybean seed and processed commodities; therefore, processing factors could not be calculated. An acceptable method was used for quantitation of residues, and the sample storage conditions and durations are supported by adequate storage stability data.

E. REFERENCES

DP#:	263245
Subject:	Product Chemistry Review of Mesotrione (ZA 1296 Technical (dry)).
From:	H. Podall
To:	J. Tompkins/J. Stone
Date:	24-FEB-2000
MRID#s:	44373503-44373505, 44505003, 44505004, and 44901701
DP#s:	245477 and 260267
Subject:	PP#: 8F04954. Mesotrione in/on Field Corn. Evaluation of Residue Data and Analytical Methods. PC Code: 122990. Case #: 289589. Submission #s: S541377 and S569871.
From:	S. Levy
To:	J. Stone/J. Tompkins
Date:	6-JUN-2001
MRID(s):	44505118, 44505212-23, 44537109-12, 44901719, and 44942401-03

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number: 8F7456
DP#: 358159
PC Code: 122990

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